

Amendments to the Specification:

Please replace paragraphs [6] and [7] with the following amended paragraphs:

[6] There are two major types of such signal transduction in mammalian cells: (i) the transmembrane protein may have a protein kinase activity in its cytosolic domain, the activity of which is activated when the extracellular substance binds to the transmembrane protein (the kinase then phosphorylates its own cytoplasmic domain, which enables the transmembrane protein to associate and activate another protein, which in turn acts on other proteins and substances within the cell cytoplasm); and (ii) the transmembrane protein may interact with a G protein that is associated with the membrane, which causes the GDP (guanine diphosphate) bound to the G protein to be replaced by GTP, resulting in dissociation of the G protein into monomer and dimer fragments, one or both of which, in turn, acts upon a target protein (also often associated with the membrane, requiring it [[too]] to then [[to]] act upon yet another target protein, this one in the cytoplasm).

[7] The physical transfer of material across the cell membrane permits a wide range of substances to get into and/or out of a cell, including ions, small molecules (such as sugars and hormones) and macromolecules (such as proteins and enzymes). Three major routes exist for such material transfer(s): (i) proteins, resident in the cell membrane may form channels that permit the passage of ions, such as sodium, potassium and ~~chlorine~~ chloride, from the extracellular milieu through the membrane and into the cytoplasm, or vice versa; (ii) proteins resident in the cell membrane may bind small molecules, such as sugars, on one side of the

membrane and then release that same molecule on the opposite side of the membrane, thereby acting as transporters; and (iii) proteins resident in the cell membrane may bind small molecules and so trigger the process of internalization, in which the bound protein:molecule pair is brought into the cell by endocytosis (at some point, the protein:molecule pair becomes separated; the protein may then be returned to the cell surface to interact with another small molecule or it may be degraded).

Please replace paragraph [20] with the following amended paragraph:

[20] A third embodiment of the present invention is directed to a method for identifying an agent that blocks an ion channel in a mammalian cell, comprising: (i) performing the method of the first embodiment of the present invention described above to determine if the agent alters the level of expression of the ion channel; (ii) performing a Western blot assay to determine if the agent alters maturation of the ion channel; and (iii) performing a tail current assay to determine if the agent alters the functional effect [[of]] on the ion channel.

Please replace paragraphs [25] and [26] with the following amended paragraphs:

[25] Binding is often easier to detect in systems in which at least one of the candidate ~~compound~~ compounds and the protein of interest [[is]] are labeled (e.g., with fluorescence, radioactivity, an enzyme, an antibody, etc., including combinations thereof, as known to those skilled in the art). After exposing the candidate compound to the cell expressing a protein and

washing off or otherwise removing unbound reagents, the presence of the labeled moiety (*i.e.*, bound to the unlabelled component of the test system) is measured.

[26] Methods for performing various binding assays are known in the art, including but not limited to the assay systems such as those described in PCT Application US98/18368. Various references provide general descriptions of various formats for protein binding assays, including competitive binding assays and direct binding assays, (*see e.g.*, Stites and Terr, *Basic and Clinical Immunology*, 7th ed. (1991); Maggio, *Enzyme Immunoassay*, CRC Press, Boca Raton, FL (1980); and Tijssen, *Practice and Theory of Enzyme Immunoassays*, in *Laboratory Techniques in Biochemistry and Molecular Biology*, Elsevier Science Publishers, B.V. Amsterdam, (1985)).